medium causing destabilization of cell membranes,

- sing destabilization of cell membranes, bonding to the said polymer, are not active with the recognition signal recognized by a cell membrane receptor and optionally having at least one free NH3+,
- the free NH₃⁺ of the said monomer optionally substituted with a non-charged residue causing a reduction in the positive charge of the polymeric conjugate which facilitates salting out of the nucleic acids upon dissociation of the complex,
- the non-charged residues having at least one -OH and are not active with the recognition/signal recognized by a cell membrane receptor

and optionally containing a molecule with a recognition signal recognized by a cell membrane receptor by substitution of some of the free NH3+ of the monomer or some of the non-charged residues causing a reduction in the positive charge or on some of the residues causing a destabilization of cell membranes or on some of the residues can sing a destabilization of cell membranes by substitution of the optional free NH3+

- with the proviso that all the free NH3+ make up at least 30% of the number of monomers of the skeleton of the polymeric conjugate,
- The complex of claim 22 wherein the substitution of the free NH3+ of the monomer is about 35%.--

--24. A complex comprised of at least one negatively charged nucleic acid and at least one positively charged polymeric conjugate with the bond therebetween being electrostatic in nature,

the polymeric conjugate containing a polymer formed from monomers having free $\mathrm{NH_3}^+$ groups, at least 10% of which are substituted by residues which can be protonated in a weakly acid medium causing destabilization of cell membranes

- said residues also comprising a functional group for bonding to the said polymer, are not active with the recognition signal recognized by a cell membrane receptor and are bases with a pH in one aqueous medium less than 8 wherein more than 50% of the bases bonded to a cationic polymer is not protonated in a medium with a pH of 7.4
- the free NH₃⁺ of the said monomer optionally substituted with a non-charged residue causing a reduction in the positive charge of the polymeric conjugate which facilitates salting out of the nucleic acids upon dissociation of the complex,
- the non-charged residues having at least one -OH and are not active with the recognition signal required by a cell membrane receptor

and optionally containing a molecule with a recognition signal recognized by a cell membrane receptor by substitution of some of the free $\mathrm{NH_3}^+$ of the monomer or some of the non-charged residues causing a reduction in the positive charge or on some of the residues causing a destabilization of cell membranes or on some of the residues causing a destabilization of cell membranes by

substitution of the optional free NH,+

- with the proviso that all the free $\mathrm{NH_3}^+$ make up at least 30% of the number of monomers of the skeleton of the polymeric conjugate.--
- --25. A complex comprising of at least one negatively charged nucleic acid and at least one positively charged polymeric conjugate with the bond therebetween being electrostatic in nature,

the polymeric conjugate containing a polymer formed from monomers having free $\mathrm{NH_3}^+$ groups, at least 10% of which are substituted by residues which can be protonated in a weakly acid medium causing destabilization of cell membranes,

- said residues also belong to a family of compounds with a nucleus selected from the group consisting of imidazole, quinoline, pterines and pyridines carrying a functional group for bonding to the said polymer, are not active with the recognition signal recognized by a cell membrane receptor and having at least one free $\mathrm{NH_3}^+$
- the free NH₃⁺ of the said monomer optionally substituted with a non-charged residue causing a reduction in the positive charge of the polymeric conjugate which facilitates salting out of the nucleic acids upon dissociation of the complex,
- the non-charged residues having at least one -OH and are not active with the recognition signal recognized by a cell membrane receptor

and optionally containing a molecule with a recognition

signal recognized by a cell membrane receptor by substitution of some of the free NH₃⁺ of the monomer or some of the non-charged residues causing a reduction in the positive charge or on some of the residues causing a destabilization of cell membranes or on some of the residues causing a destabilization of cell membranes by a substitution of the optional free NH₃⁺

- with the proviso that all the free $\mathrm{NH_3}^+$ make up at least 30% of the number of monomers of the skeleton of the polymeric conjugate.--

--26. The complex of claim 22 wherein the residue causing destabilization of cell membranes in a weakly acid medium are selected from the group consisting of alkylimidazole with 1 to 10 alkyl carbon atoms and one nitrogen atom of the imidazole is substituted and a quinoline of the formula

wherein R_1 is hydrogen and R_2 is $-(CH_2)_n$ -COOH and n is an integer from 1 to 10.--

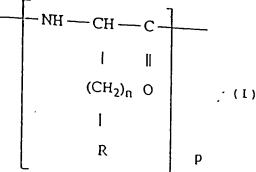
--27. The complex of claim 26 wherein the said residue is selected from he group consisting of histidine, 4-carboxymethyl-

imidazole, 3-(1-methyl-imidazol-4-yl)-alanine, 3-(3-methyl-imidazol-4-yl)-alanine, 2-carboxy-imidazole, histamine, 3-(imidazol-4-yl)-L-lactic acid, 2-(1-methyl-imidazol-4-yl)ethylamine, 2-(3-methyl-imidazol-4-yl)ethylamine, β-alanyl-histidine-(carnosine), 7-chloro-4-(amino-1-methylbutylamino)-quinoline, N⁴-(7-chloro-4-quinolinyl)-1,4-pentanediamine, 8-(4-amino-1-methylbutylamino)-6-methoxyquinoline (primaquine), N⁴-(6-methoxy-8-quinolinyl)-1,4-pentanediamine, quininic acid, quinolinecarboxylic acid, pteroic acid, nicotinic acid and quinolinic acid.--

191

--28. The complex of claim 26 wherein the said residue has an imidazole nucleus and the remaining free NH₃⁺ of the monomer are 1 to 60% substituted with a molecule with a molecular weight of less than 5000 and having a recognition signal recognized by a cell membrane receptor optionally present in an amount of one molecule per 200 units of polymeric conjugate.--

--29. The complex of claim 22 wherein the polymer has a grouping of the formula $-\begin{bmatrix} NH - CH - C \end{bmatrix}$



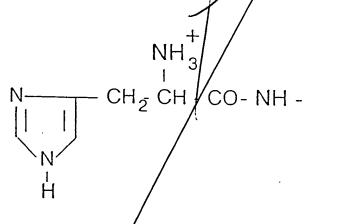
wherein p is an integer of 15 to 900, n is an integer from 1

to 6 and 10 to 45% of the R being a residue with an imidazole nucleus and optionally by a molecule having a recognition signal,

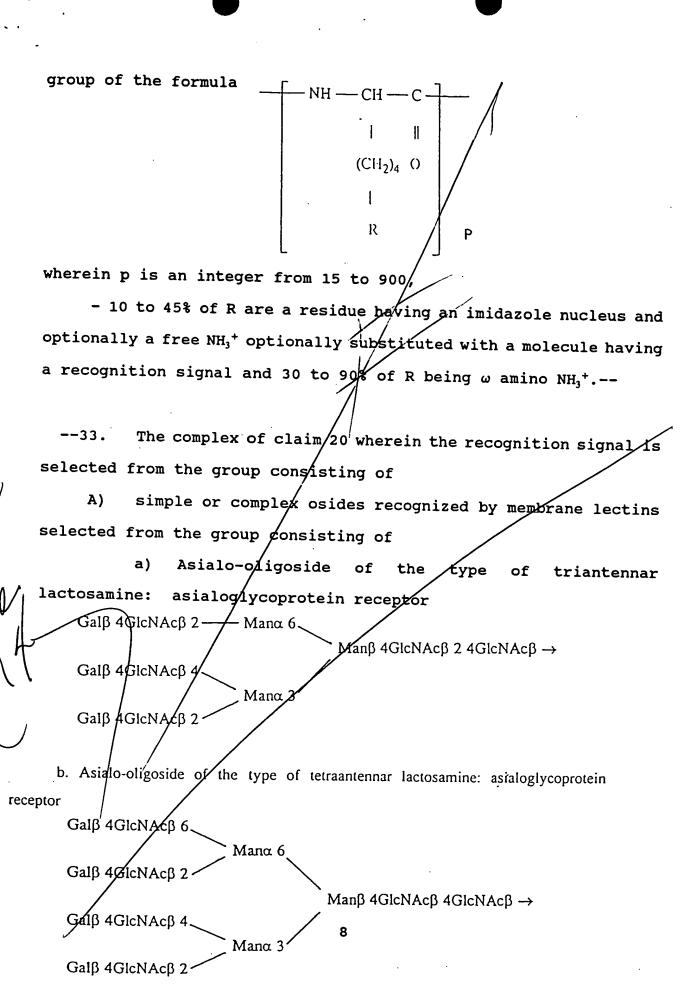
- 10 to 90% of R being free ω -amino NH₃⁺ optionally substituted 0 to 50% by a molecule having a recognition signal for at least one molecule for 200 units

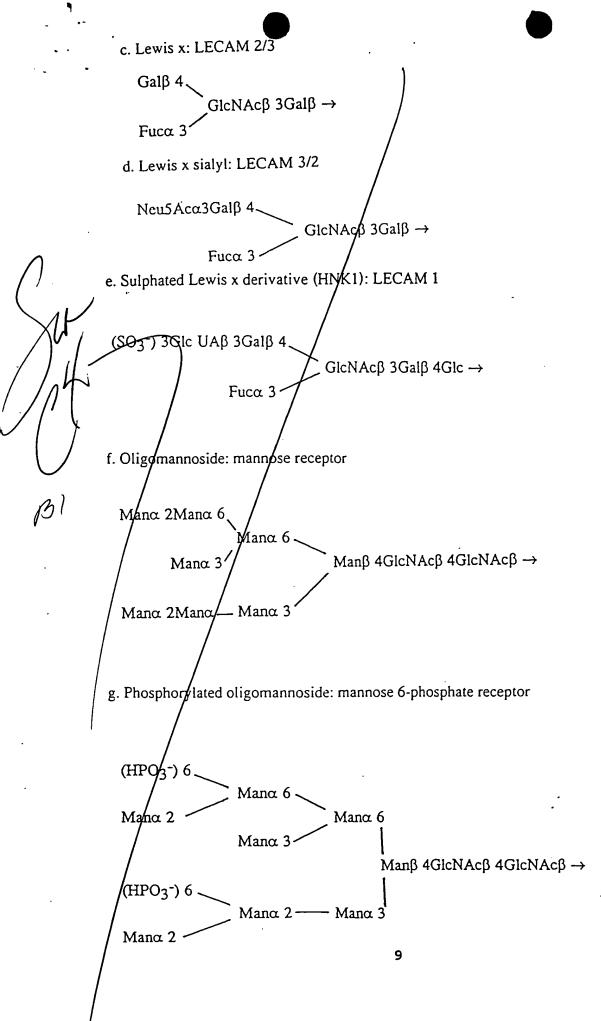
and optionally 0 to 45% of R being $-NH-CO-(CHOH)_m-R_1$, m is an integer from 2 to 15 and R_1 is hydrogen or alkyl of 1 to 15 carbon atoms optionally substituted with a molecule having a recognition signal.--

--30. The complex of claim 27 wherein R has the formula



- --31. The complex of claim 27 wherein m is 2 to 7 -NH-CO- $(CH_2OH)_m$ -R₁ and is selected from the group consisting of a dihydroxypropionylamido, erythronylamido, threonylamido, ribonylamido, arabinylamido, xylonylamido, lyxonylamido, gluconylamido, galactonylamido, mannonylamido, glycoheptonylamido and glycooctonylamido.--
 - --32. The complex of claim 27 wherein the polymer has a polymer





h. Oligosaccharide of the type of sulphated lactosamine: sulphated GalNAc 4/eceptor (SO₃⁻) 4GlcNAcβ 4GlcNAcβ 2Manα 6. Manβ 4GlcNAcβ ★GlcNAcβ → → (SO₃-) 4GlcNAcβ 4GlcNAcβ 2Manα 3-B) Pept des anti-inflammatory peptides or certain of their fragments recognized by receptors of the vascular wall selected from the group consisting of vasodilator intestinal polypeptide (VIP) HSDAVFTDNYTRLRKQMAVKYLNSILN-NH, atrial natriuretic polypeptide (ANP) SLRRSSCFGGRMDRIGAQSGLGCNSFRY - lipocortin HDMNKVLDL and - bradyk*i*nin RPPGFSPFR; ligand peptides of integrins containing the sequence RGD, fibronectin ligand;

- c) chemiotactic factors, formyl-peptides and their antagonists: FMLP, (N-formyl-Met-Leu-Phe);
 - d) peptide hormones,

α-MSH: Ac-SYSMEHFRWGKPV-NH2 and their antagonists;

natural metabolites selected from the group consisting of

- biotin,
- carnitine
- tetrahydrofolate and folic acid, which can be both a recognition signal with respect to certain cells having suitable receptors and a destabilizer of cell membranes.--

--34. Complex of claim 22 wherein the nucleic acid is selected from the group consisting of

- a) marker genes,
 - genes containing luciferage,
 - green protein of the jellyfish Aequarea victoria,
 - genes containing β -galactosidase,
- genes containing ehloramphenicol acetyl-transferase,

and genes which confer resistance to an antibiotic,

- b) genes with a therapeutic purpose selected from the group consisting of hypercholesterolaemia,
 - coagulation factors: factors VIII and IX,
 - phenylalahine hydroxylase (phenylketonuria),
 - adenosine deaminase (ADA immunodeficiency),

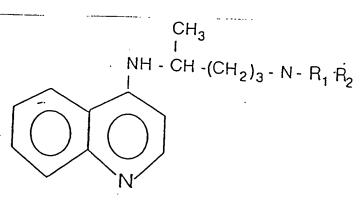
- lysosomal enzymes, such as β -glucosidase in the case of Gaucher's disease,
 - dystrophin and minidistriphin (myopathy),
 - tyrosine hydroxylase (Parkinson),
 - neurone growth factors (Alzheimer),
- CFTR cystic fibrosis tránsmembrane conductance regulator (cystic fibrosis),
 - alpha-1-antitrypsin,
- cytokines (interleukins, TNF tumor necrosing factor),
 - thymidine kinase of the Herpes simplex virus,
- proteins of MHC, major histocompatibility complex, in particular HLA-B7,
 - cytosine deaminase,
 - genes which code for sense and antisense RNAs, and
 - genes which code for ribozymes, and
 - c) genes which code for viral antigens (vaccination).--
 - --35. The complex of claim 22 wherein:
- the polymer has a degree of polymerization of about 15 to about 900,
- the free $/{\rm NH_3}^+$ functions of the lysine units being substituted in a ratio of 35% by histidyl residues and optionally by a molecule which constitutes a recognition signal for 1 to 50 residues of lysine, where the said signal molecule has an affinity of at least 10 5 møle $^{-1}$ with respect to the receptor of the cell which

the complex is to target, or optionally by 20 to 100 molecules of recognition signal for 200 lysine residues, where the said signal molecule has an affinity of less than 10⁵ mole⁻¹ with respect to the said receptor,

- the nucleic acid has a molecular weight of about 106 to about 108,
- the ratio between the average number of base pairs of the nucleic acid per molecule of monomer unit, is about 0.2 to about 6.--
- --36. Positively charged polymeric conjugate containing monomer units having free NH₃⁺:
- the free $\mathrm{NH_3}^+$ functions of the monomer units being at least 10% by residues causing a destabilization of cell membranes in a weakly acid medium,
- the said residues carrying a functional group to be bonded to the above-mentioned polymer,
- are not active with a recognition signal recognized by a cell membrane receptor and having at least one free NH₃⁺;
- the free $\mathrm{MH_3}^+$ of the monomer units optionally substituted by non-charged residues causing a reduction in the positive charges with respect to the same unsubstituted polymeric conjugate, facilitating salting out of the nucleic acid by dissociation of the complex,
- the non-charged residues also having at least one hydroxyl, are not active with respect to the recognition signal recognized by

a cell membrane receptor,

- optionally the hydroxyl groups of the non-charged residues are substituted by at least one molecule having a recognition signal recognized by a cell membrane receptor, and optionally containing a molecule with a recognition signal recognized by a cell membrane receptor by substitution of some of the free NH₃⁺ of the monomer or some of the non-charged residues causing a reduction in the positive charge or on some of the residues causing a destabilization of cell membranes or on some of the residues causing a destabilization of cell membranes by substitution of the optional free NH₃⁺
- with the proviso that all the free NH₃⁺ make up at least 30% of the number of monomers of the skeleton of the polymeric conjugates.--
- --37. The polymeric conjugate of claim 36 wherein the residue causing destabilization of cell membranes in a weakly acid medium are selected from the group consisting of alkylimidazole with 1 to 10 alkyl carbon atoms and one nitrogen atom of the imidazole is substituted and a quinoline of the formula



wherein R_1 is hydrogen and R_2 is $-(CH_2)_n$ -COOH and n is an integer from 1 to 10.--

- --38. The method of claim 21 wherein the cells are selected from the group consisting of
 - cells of haematopoietic strains;
 - dendritic cells;
 - liver cells;
 - skeletal muscle cells;
 - skin cells;
 - · fibroblasts,
 - · keratinocytes,
 - · dendritic cel/15
 - · melanocytes
 - cells of the vascular walls;
 - · endothelial:
 - smooth muscle;
 - epithelial cells of the respiratory tract;
 - cells of the central nervous system;
 - cancerous cells and
 - cells of the immune system. --
- --39. A method of transfecting cells comprising contacting the cells in a medium with a complex of claim 22 whereby the complex passes into the cytoplasm of the cells, salting out the nucleic acid from the complex in the cytosol and/or the nucleus of the

cells, transcription and expression of the nucleic acid in the transfected cells and expression of the protein corresponding to the transfected gene.--

- substituted by a residue causing destabilization of cell membranes in a weakly acid medium and optionally carrying a recognition signal being a function of a target cell optionally bonded beforehand to the polymer conjugate 2) optionally a plasmid containing at least one gene to be transferred and optionally a system for regulation of the expression of the said gene, 3) reagents allowing optional bonding of the recognition signal to the polymeric conjugate, 4) reagents for effecting the formation of a complex of claim 22 or a complex of the polymeric conjugate and the plasmid containing the gene to be transferred and 5) reagents for transection of the cell by the complex of claim 22.—
- --41. A vaccine against influenza comprising an antivirally effective amount of a posivitely charged polymeric conjugate of claim 36 and an inert pharmaceutical carrier.--
- --42. A method of protecting a warm-blooded animal from influenza comprising administering to a warm-blooded animal an antivirally effective amount of a positively charged polymeric conjugate of claim 36.--